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Specific depletion of myelin-reactive B cells via BCR-targeting

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Abstract

© 2015 Park-media, Ltd. B cells play a crucial role in the development and pathogenesis of systemic and organ-specific autoimmune diseases. Autoreactive B cells not only produce antibodies, but also secrete pro-inflammatory cytokines and present specific autoantigens to T cells. The treatment of autoimmune diseases via the elimination of the majority of B cells using the monoclonal anti-CD19/20 antibody (Rituximab) causes systemic side effects and, thus, requires a major revision. Therapeutic intervention directed towards selective elimination of pathogenic autoreactive B cells has the potential to become a universal approach to the treatment of various autoimmune abnormalities. Here, we developed a recombinant immunotoxin based on the immunodominant peptide of the myelin basic protein (MBP), fused to the antibody Fc domain. We showed that the obtained immunotoxin provides selective in vivo elimination of autoreactive B cells in mice with experimental autoimmune encephalomyelitis. The proposed conception may be further used for the development of new therapeutics for a targeted treatment of multiple sclerosis and other autoimmune disorders.

Keywords

Autoantigens, B cells, Immunoglobulins, Immunotoxins, Multiple sclerosis